Formulation and Evaluation of Etoricoxib Emulgel.

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ABSTRACT

Etoricoxib, a selective COX-2 inhibitor, is widely used for managing inflammatory conditions such as osteoarthritis and rheumatoid arthritis. However, its oral administration is associated with gastrointestinal side effects and limited bioavailability. This study focuses on developing a topical emulgel formulation of Etoricoxib to enhance its therapeutic efficacy while minimizing systemic side effects. The emulgel combines the advantages of both emulsions and gels, offering improved drug penetration and patient compliance. The formulation was optimized using various gelling agents and evaluated for physicochemical properties, in vitro drug release, skin permeation, and anti-inflammatory activity. The optimized emulgel demonstrated satisfactory pH, viscosity, drug content, and enhanced anti-inflammatory effects, indicating its potential as an effective topical delivery system for Etoricoxib.

Keywords: Etoricoxib,Topica[drug delivery,NSAIDs, emulgel,in-vitro drug release, Franz diffusion method, skin permeation, drug formulation.

1. INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used for the treatment of pain and inflammation associated with conditions such as osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis. Etoricoxib is a potent, selective cyclooxygenase-2 (COX-2) inhibitor that offers effective anti-inflammatory and analgesic action with reduced gastrointestinal toxicity compared to non-selective NSAIDs. Despite its clinical efficacy, oral administration of Etoricoxib can still lead to systemic side effects, including cardiovascular and gastrointestinal complications, particularly with long-term use.

To overcome these limitations, topical drug delivery systems have gained significant attention, offering site-specific action with minimal systemic absorption. Among these, emulgels—a combination of emulsion and gel—have emerged as promising carriers for hydrophobic drugs like Etoricoxib. Emulgels offer the advantages of improved drug solubilization, controlled release, enhanced skin penetration, and better patient compliance due to their non-greasy texture and ease of application.

This study aims to develop and evaluate a topical emulgel formulation of Etoricoxib using suitable gelling agents and emulsifying components. The formulation was characterized for its physicochemical properties, drug release behavior, skin permeation capability, and anti-inflammatory efficacy to assess its potential as an alternative to oral NSAID therapy.

2. AIM, OBJECTIVE AND NEED OF STUDY :

AIM:

Formulation And Evaluation Of Emulgel Using Model Drug.

OBJECTIVES:

- To enhance patient compliance.
- To improve the penetration and absorption of poorly water-soluble drugs through the skin.
- To prevent first-pass metabolism.
- To overcome the limitation of conventional oral and parenteral route of drug administration.
- To eliminate the drawbacks of emulsion and gel by formulating in an Emulgel.

3. Materials and Methods

3.1 Materials:

Gelling Agents: Carbopol 940/934, Hydroxypropyl methylcellulose (HPMC) K4m

Emulsifiers: Span 80, Tween 80

Oil Phase: Castor oil, liquid paraffin

Co-surfactant: Polyethylene glycol (PEG) 400

Other Excipients: Propylene glycol, Triethanolamine, Distilled water

3.1.2 PREFORMULATION STUDIES

Solubility studies were conducted to determine the solubility of Etoricoxib in various oils, surfactants, and co-surfactants.Castor oil was selected as the oil phase due to its high solubilizing capacity for Etoricoxib. Tween 80 and PEG 400 were chosen as surfactant and co-surfactant, respectively, based on their emulsifying properties and compatibility.

3.1.3 ANALYTICAL CHARACTERIZATION OF DRUG SAMPLE:

Various drug concentrations (2-10ug/ml) in buffer were prepared and the absorbance was measured at 284 nm. For the standard curve, 25mg of Etoricoxib was accurately weighed and dissolved in 25 ml of 6.8 ph buffer, Pipette out 0.2ml this resulting solution and further diluted to 100ml with buffer to make stock solution of concentration 2ug/ml. Further serial dilutions were prepared with buffer to get concentrations 2, 4, 6, 8 and 10ug/ml. The absorbance was measured against 6.8 pH buffer at 284 nm using UV/Visible spectrophotometer. The plot of absorbance concentration was plotted and subjected to linear regression analysis. The absorption maxima of Etoricoxib was determined by scanning the sample drug solution concentration in double beam UV spectrophotometer for range of 284 nm and standard specification given in Indian pharmacopoeia or literature.

3.1.4 Formulation of Emulgel:

A nanoemulsion of Etoricoxib was prepared using the spontaneous emulsification technique. The oil phase (Castor oil and liquid paraffin containing Etoricoxib) was mixed with the Span 80. Mix (Tween 80 and PEG 400) and added to the aqueous phase under continuous stirring. The resulting nanoemulsion was incorporated into a gel base prepared with Carbopol 940/934 and HPMC K4M, neutralized with triethanolamine to obtain the final emulgel formulation.

Table No. 1: Different batches of Emulgel formulation from F1 to F8

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Etoricoxib (mg)	300	300	300	300	300	**300**	300	300
Carbopol940(mg)	400	_	_	_	200	**200**	300	200
Carbolpol934(mg)	_	400	_	_	_	**_**	_	_
Xanthum gum (mg)	_	_	500	_	_	**_**	_	_
HPMC (mg)	_	_	_	300	_	**_**	_	200
Sodium Aginate (mg)	_	_	_	_	200	**_**	_	_
Castor oil (ml)	3	3	3	3	3	**3**	3	3
Liquid paraffin (ml)	3	3	3	3	3	**3**	3	3
Span 80 (ml)	1.5	1.5	1.5	1.5	1.5	**1.5**	1.5	1.5
Tween 80 (ml)	1.5	1.5	1.5	1.5	1.5	**1.5**	1.5	1.5
Propylene glycol (ml)	1.5	1.5	1.5	1.5	1.5	**1.5**	1.5	1.5
Polyethylene glycol 400 (ml)	1.5	1.5	1.5	1.5	1.5	**3**	3	3
Ethanol (ml)	2	2	2	2	2	**2**	2	2
Triethanolamine (ml)	q.s	q.s	q.s	q.s	q.s	**q.s**	q.s	q.s
Methyparaben (ml)	0.06	0.06	0.06	0.06	0.06	**0.06**	0.06	0.06
Water (ml)	q.s	q.s	q.s	q.s	q.s	**q.s**	q.s	q.s

4. EVALUATION PARAMETERS

4.1.1 Physical Appearance:

Color, consistency, and homogeneity

4.1.2 pH Measurement:

The pH values of all the formulations where measured by immersing the electrode directly into the dispersion using calibrated pH meter.

4.1.3 Viscosity:

Measured using a Brookfield viscometer

4.1.4 Drug Content:

1 gram of the Etoricoxib emulgel formulation was accurately weighed and transferred into a 100 mL volumetric flask. To this, 1 mL of ethanol was added to aid in the solubilization of the drug. The volume was then made up to 100 mL using phosphate buffer (pH 6.8) and the solution was thoroughly mixed. The resulting solution was filtered using Whatman filter paper No. 41 to remove any particulate matter.

From the filtrate, 1 mL was pipetted and further diluted to 10 mL with phosphate buffer (pH 6.8). The absorbance of the final solution was measured at 284 nm using a UV-Visible spectrophotometer against a blank of phosphate buffer pH 6.8.

4.1.5 Spreadability:

Assessed by the slip and drag characteristics of the formulation

4.1.6 In vitro diffusion studies:

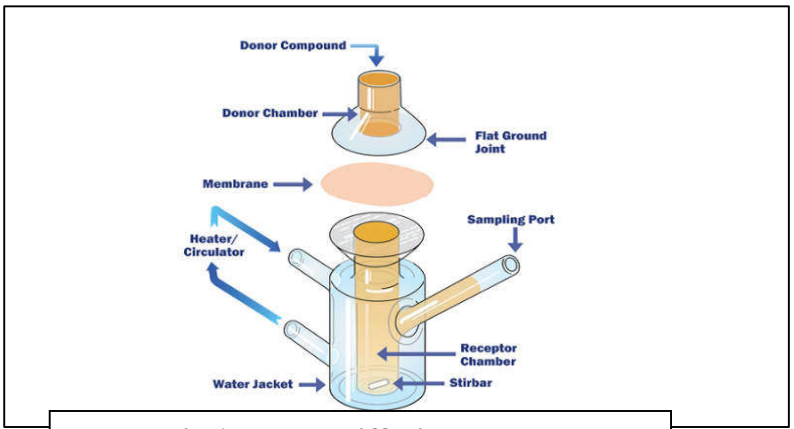

Fig 1 :Franz Diffusion cell

In-vitro diffusion study of emulgel formulation was performed through the cellulose membrane by using Franz diffusion cell. The receptor compartment was filled with 6.8 pH phosphate buffer and kept at 32 ± 0.5 °C with continuous stirring with help of a magnetic stirrer. 500mg of the emulgel was placed over the cellulose membrane. An interval of 60min, and upto 8 hours ,2 ml sample was withdrawn and suitably diluted. The withdrawn samples where replaced with the same amount of 6.8 pH phosphate buffer to maintain the sink condition. Diluted samples were analysed with help of UV at 284 nm.

5. RESULTS AND DISCUSSION

5.1.1 Preparation of standard calibration curve of Etoricoxib in buffer 6.8:

Table No. 2 : Calibration curve of Etoricoxib in phosphate buffer of pH 6.8.

Concentration (ug/ml)	Absorbance (at 284 nm)
2	0.125
4	0.245
6	0.368
8	0.491
10	0.612

Correlation Co-efficent: R^2-0.9994

Equation of regression line: y= 0.061x + 0.0044

Where, X Value of concentration

Y = Regression value of absorbance

5.1.2 Standard Calibration Curve of Etoricoxib in Phosphate buffer pH 6.8:

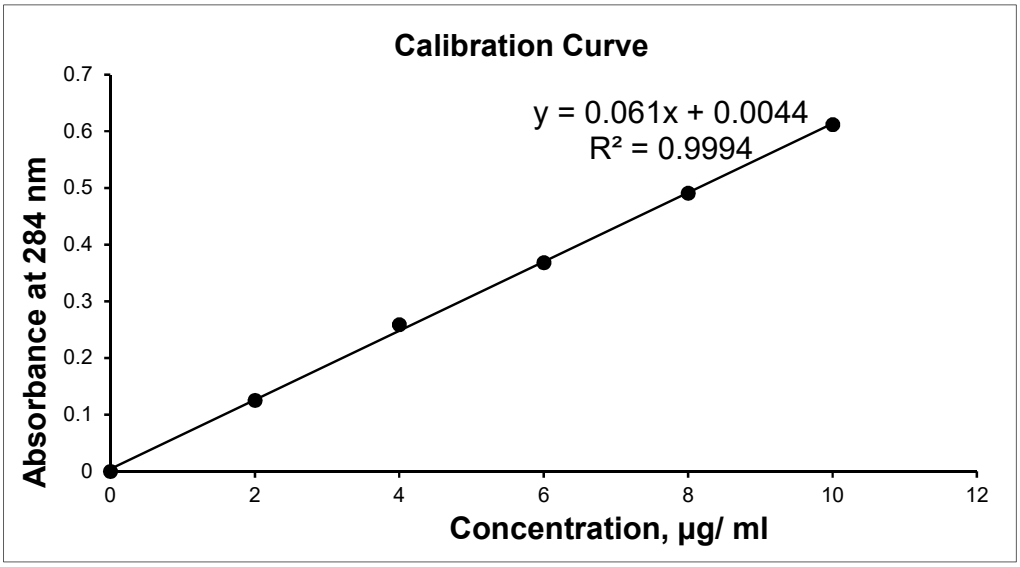

Fig. 2: Standard Calibration Curve of Etoricoxib in Phosphate buffer of pH 6.8.

5.1.3 Drug-Excipients Compatibility Studies Using FTIR:

5.1.3.1 FTIR of pure Etoricoxib:

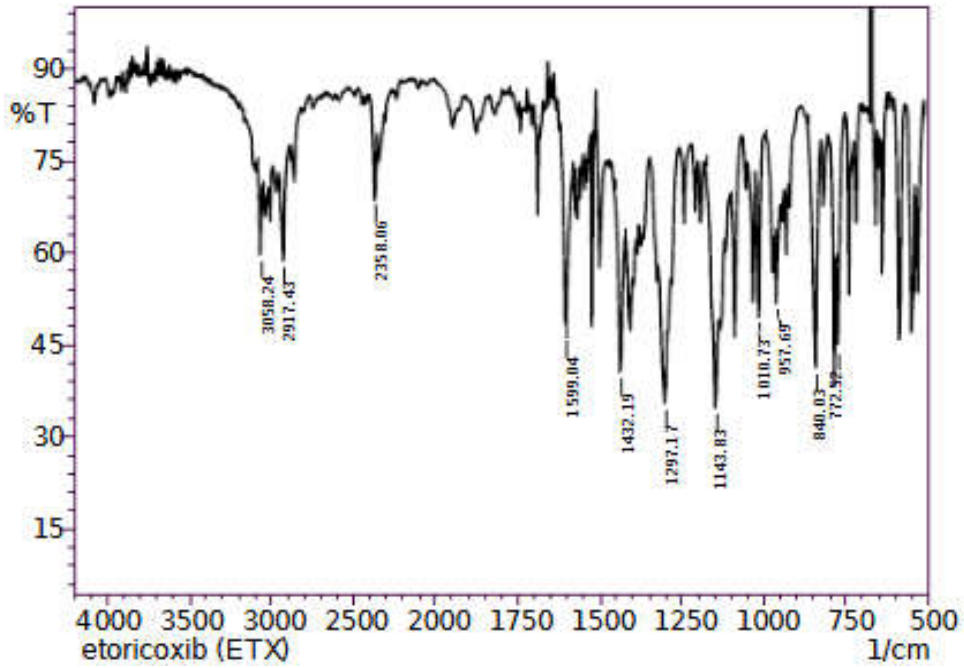

Fig. 3: IR spectra of Etoricoxib

Table No. 3 : Table Showing FTIR Peaks of Etoricoxib

Sr. No.	Peaks Observed in IR Spectra of Etoricoxib	Functional Group
2	2917.45	Aliphatic C–H Stretching.
4	1599.04	Aromatic C=C Stretching.
5	1432.19	CH_2 bending or aromatic ring.
6	1297.17	C–N or S=O Stretching.
7	1143.83	C–O–C (ether) or S=O Stretching.
8	1010.27	C–F (if fluorine is present) or C–N Stretching.
9	957.65-840.03	C–H out-of-plane (aromatic) Bending.
10	722.59	C–H bending (alkyl chain) Rocking.

5.1.3.2 FTIR of Etoricoxib and carbapol940:

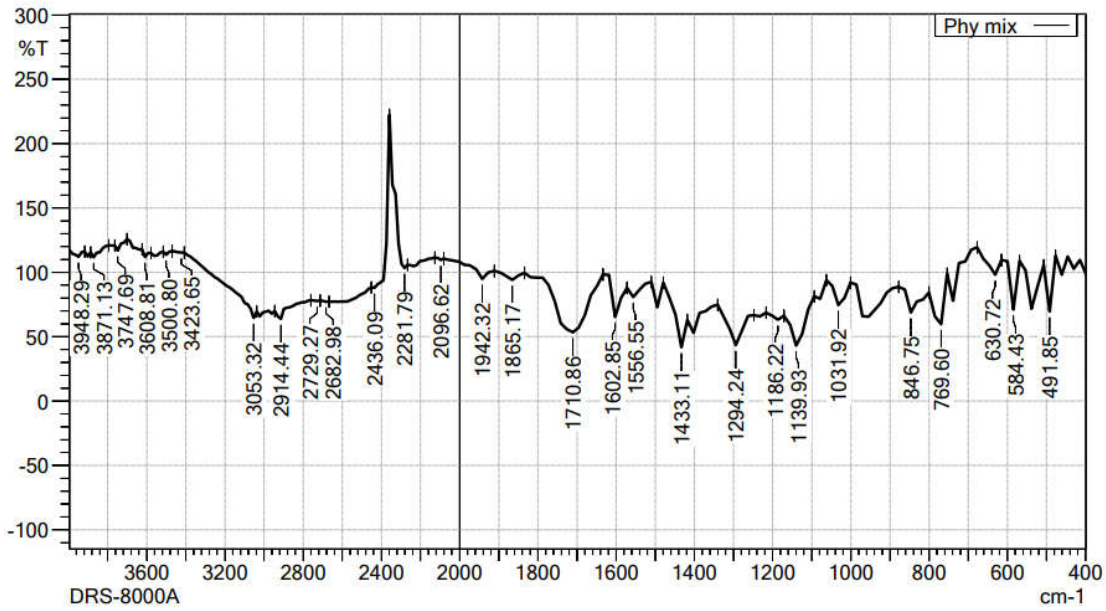

Fig. 4: IR spectra of Etoricoxib + Polymer.

Table No. 4 : Table Showing FTIR peaks of Etoricoxib + Polymer.

Sr. No.	Peaks Observed in IR Spectra of Etoricoxib+Polymer	Functional Group
1.	2917	C–H stretch (aromatic/aliphatic) Stretching (C–H).
2.	1602.85	C=C stretch Aromatic ring.
3.	1433.11	CH_2 bending / aromatic ring.
4.	1294	C–N or S=O stretch / C–O–C.
5.	1139	C–N or S=O stretch / C–O–C.
6.	1031.92	C–F or C–O stretch.
7.	846.75	C–H out-of-plane (aromatic).
8.	769.60	C–H out-of-plane (aromatic).

6. EVALUATION OF ETORICOXIB EMULGEL

6.1.1 Physical Appearance:

The formulated emulgel was white, homogeneous, and free from any grittiness.

6.1.2 pH:

The pH of the formulation was found to be in the range of 6.8 to 7.1, which is compatible with skin pH, suggesting minimal risk of irritation upon application**.**

6.1.3 Viscosity:

The viscosity of the emulgel was within acceptable limits, ensuring adequate consistency for topical application.

6.1.4 Spreadability:

The formulation exhibited good spreadability, indicating ease of application and better patient compliance.

6.1.5 Drug Content:

The drug content of the emulgel was found to be 93.54 ± 1.26%, indicating uniform distribution of Etoricoxib within the formulation.

6.1.6 In Vitro Drug Release:

The in-vitro drug release study was carried with the help of Franz diffusion cell apparatus. And cumulative % drug release was obtained, which shows in below the table No. and Batch F6 was obtained optimized batch. Release of the drug from the formulation was depended on the nature and concentration of polymer. Formulation with carbopol 940 showed the good drug releasing properties. This comparative drug diffusion study was performed to compare the percent drug release between the different batches. Hence the objective of improving solubility and diffusion of drug through the skin by formulating into Emulgel formulation has been achieved.

Table No. 5 : In-Vitro Drug diffusion study profile of formulation F1 to F8.

Time (hr)	F1 %CDR	F2 %CDR	F3 %CDR	F4 %CDR	F5 %CDR	F6 %CDR	F7 %CDR	F8 %CDR
1	13.75	17.15	12.97	13.30	12.60	**16.07**	11.75	18.16
2	20.87	24.86	20.06	19.61	20.77	**28.68**	25.37	25.19
3	25.23	33.03	23.40	30.32	26.56	**40.02**	37.04	30.35
4	34.33	39.77	31.25	39.11	34.95	**48.12**	48.50	40.07
5	44.22	50.00	40.36	50.32	45.82	**61.80**	58.87	50.33
6	53.92	58.27	45.04	61.85	55.64	**70.67**	63.85	60.52
7	61.57	68.08	55.77	70.30	68.65	**81.07**	77.09	72.22
8	69.57	77.34	65.59	73.34	81.04	**91.05**	84.94	81.14

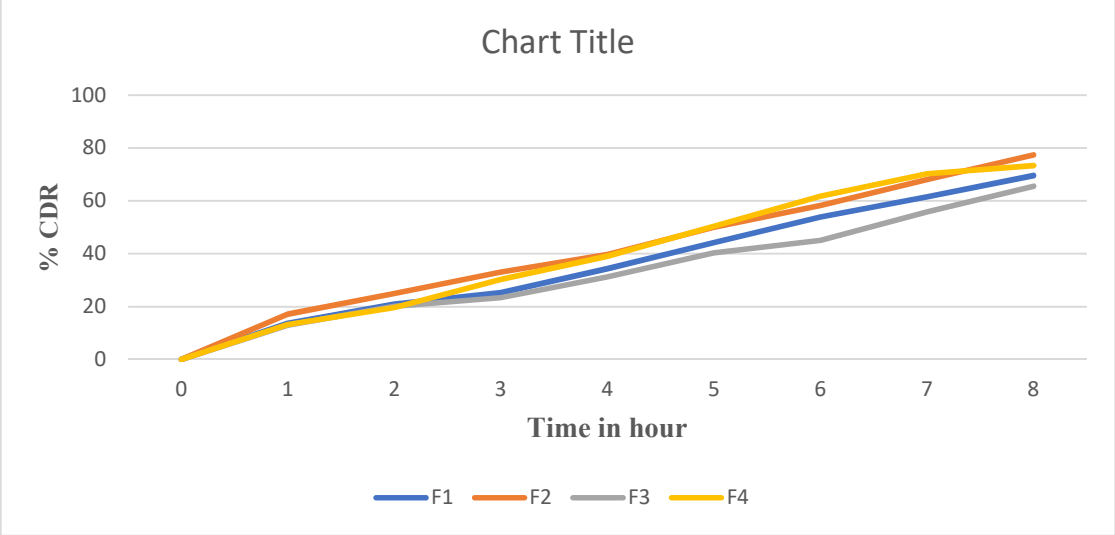

Fig. 5: Diffusion study of emulgel containing Etoricoxib of Formulation F1-F4.

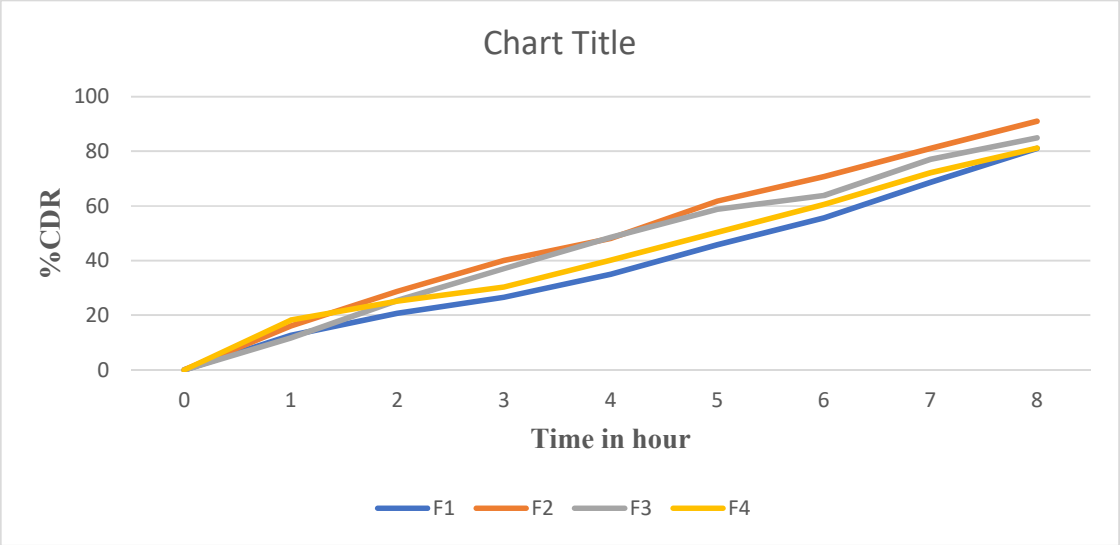

Fig. 6: Diffusion study of emulgel containing Etoricoxib of Formulation F5-F8.

The in vitro drug release study demonstrated a biphasic release pattern with an initial burst release followed by a sustained release phase. Approximately 91.3 ± 1.8% of Etoricoxib was released over 8 hours, indicating the potential for prolonged therapeutic effect.

7. Optimization of batches:

From all the formulation of 8 batches one batch F6 is our optimize batch because it has shown better **Spreadability : 23.96 gm.cm/sec, Viscosity : 3921 cps, High diffusion : 91.05%, pH : 6.9 and Stability.**

8. Summary and Conclusion:

The present study successfully demonstrated the formulation and evaluation of an Etoricoxib emulgel as an effective topical drug delivery system for anti-inflammatory therapy. The prepared emulgel formulations showed desirable physicochemical properties such as acceptable pH, physical appearance, and stability, making them suitable for application on the skin.

The combination of emulsion and gel not only enhanced the drug release profile but also improved patient compliance by offering ease of application, non-greasy texture, and sustained drug release at the site of inflammation. The dual-controlled release system of emulgel provides a promising platform for the topical delivery of hydrophobic drugs like Etoricoxib.

Thus, it can be concluded that Etoricoxib emulgel is a stable, effective, and patient-friendly formulation and can be further explored for its therapeutic potential in the treatment of inflammatory conditions.

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